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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/632,878
Filing Date: August 01, 2003
Appellant(s): GELBER ET AL.

Rivka D. Monheit
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed October 22, 2007 appealing from the Office action mailed April 18, 2007.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The Appelants statement of the status of amendments contained in the brief is correct. Appelants state that a supplemental amendment was filed on October 17, 2007 (see claim 11) and that the Examiner has not indicated if the amendment would be entered.

The amendment after final rejection filed on October 17, 2007 has been entered.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The Appellants statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

Claim 11 in the Claims Appendix is the claim prior to the supplemental amendment. Since the supplemental amendment has been entered, claim 11 will be treated as the claim 11 of the October 17, 2007 claim set.

Claim 11 as entered reads as follows: The method of claim 38, wherein the immune response is measured by detecting an antibody, T cell proliferation, or production of a cytokine.

All other claims are correct.

(8) Evidence Relied Upon

The following is a listing of the evidence relied upon in the rejection of claims under appeal.

US-6,071,497 06-2000 Steiner et al. (as cited previously).

US-6,652,885 11-2003 Steiner et al. (as cited previously).

Patton, et al., "The Lungs as a Portal of Entry for Systemic Drug Delivery", Proc. Amer. Thorac. Soc., 1:338-344 (2004) (as cited by Appelant). It is noted that Appelants evidence document is post-filing date art.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1,3-6,8-18,20-24,26,28,33-36,38 are rejected under 35 U.S.C. 102(b) as being anticipated by Steiner et al. (US 6,071,497; the '497 patent).

Steiner et al. teaches methods of delivering particles across the membranes of the pulmonary system with compositions comprising diketopiperazine (DKP) of required size with agents such as insulin and calcitonin, for example (see claims 7,10,11). Specifically, Steiner et al. teach calcitonin-DKP used in mammal models (see column 11, example 1). Example 1 shows that administration can be performed directly and in vivo. In one embodiment the delivery occurs via microparticles. Although Steiner does not teach percent immune responses, Steiner teach the same compound and method steps as claimed in the instant invention; thus, the responses of the patients will be the same as instantly claimed. With regard to 'enhancing transport', the same compounds are taught and used as instantly claimed so the compounds would necessarily share the same bio-effecting characteristics. One of ordinary skill in the art would see that the two compounds of '497 and of the instant claims would have the same characteristics.

Claims 1,4-10,13-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Steiner et al. (US 6,652,885; the '885 patent).

Steiner et al. teach an insulin–DKP composition for pulmonary membrane transport (see example 2; claim 1; abstract; column 10 lines 20-34). Administration can be via inhalation or orally among others (column 10 lines 52-53). Steiner teach that 'formulations and methods also are provided for the improved transport of active agents across biological membranes' (abstract and column 3 line 42). Further, it is stated that 'the diketopiperazines also serve both to stabilize and enhance delivery to the entrapped materials. Formulations also have been developed for the

enhanced transport of active agents across biological membranes' (column 4 line 12). One of ordinary skill in the art would see that the two compounds of '885 and of the instant claims, respectively, would have the same characteristics since it is stated that diketopiperazines enhance delivery. It is also stated that, 'the compositions can be administered to any targeted biological membrane' (column 10 line 54). Since a cell membrane/lipid bilayer fall within the scope of any biological membrane, the patent clearly discloses enhanced transport across a cell membrane/lipid bilayer and delivery into a cell.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1,3-36 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steiner et al. (US 6,071,497; the '497 patent) and Steiner et al. (US 6,652,885; the '885 patent).

Both references teach compounds comprising an active agent encapsulated with DKP microparticles for administration for active targeting of pulmonary tissue wherein the compounds may be administered via inhalation or orally.

One would be motivated to combine the references because '497 itself is referenced in '885 (column 2 line 58) and mentioned as work to improve upon (column 2-3). It would have been obvious to one skilled in the art at the time of invention to determine all operable and optimum ratios, doses, rates of administration, etc. for the claimed composition of the instant

application, because the component ratios, doses, rates of administration, etc. are an art-recognized result-effective variable that is routinely determined and optimized in the composition/pharmaceutical arts. One would have an expectation for success based on the examples provided.

(10) Response to Arguments

Appelants Arguments – 102 rejections

Regarding the 102 rejection with the '497 patent (Steiner et al. (US 6,071,497; the '497 patent)), Appelants argue that the prior art does not teach the claimed method. Appelants argue that the results (column 11 lines 62-64 of '497) showing rapid absorption of the compounds into the blood do not disclose administration of a compound through a cell membrane. Appelants argue that drug transport may occur between cells and cite Patton et al. Appelants argue that the mechanism of uptake via phagocytic cells is not equivalent to transport of a compound across a cell membrane. Appelants argue that immune system responses are not taught, specifically the achievement of the prevention of an increase in a cell's immune response. Appelants argue that the engagement/lack of engagement of a toll-like receptor is not taught.

Regarding the 102 rejection with the '885 patent (Steiner et al. (US 6,652,885; the '885 patent)), Appelants argue that the prior art does not teach the claimed method. Appelants argue that a discussion of blood plasma levels does not disclose or suggest administration of a compound through a cell membrane. Appelants argue that the '885 patent does not teach enhanced transport. Appelants argue that drug transport may occur between cells and cite Patton

et al. Appelants argue that the avoidance of immune responses are not taught. Appelants argue that engagement/lack of engagement of a toll-like receptor is not taught.

Taken together, the Appelants argue that the limitations of numerous dependent claims (claims 4,11-13,33,38) are not met.

Response to Arguments—102 rejections

Appelants argue that the disclosure does not disclose administration into a cell. The active steps of claim 1 of the current invention include the formation of a complex and contacting a cell with the complex. The '497 patent teach in example 1 the administration of salmon calcitonin-diketopiperazine (DKP) microparticles via instillation in each lung of a sheep. The '885 patent teach in example 2 the inhalation of insulin-DKP in humans. It is noted that the Appelants have not disputed the composition of the prior art. Since the active step of the claims is contacting and '497 and '885 teach administration (via instilling in '497 and via inhalation in '885) with compounds of the current invention, the contacting and transport would necessarily follow from the active steps. Appelants arguments regarding the method of measurement of absorption are not convincing since the active step taught is contacting, not measurement of absorption. The method of measurement does not negate the fact that the compounds were administered.

Further, since Appellant appears to argue that the prior art contacting steps are not necessarily contacting steps that would meet the claim limitations, it is pointed out that methods of contacting and delivery such as inhalation are taught by the Appelant (specification page 10 line 14-21). Such methods are the same as those taught in the '885 patent (example 2 and claim

3). Therefore, the Appelants are not using a special definition of 'contacting'. The broadest reasonable interpretation of the active step of 'contacting' includes the administrations as taught by the cited references ('497 in example 1; '885 in example 2 and claim 3). Accordingly, administration of the active agent via inhalation and/or installation would result in "contacting" and enhanced transport of the compound directly to the cell.

The reference cited by Appelant (Patton et al.) states that drug transfer from the lung to the blood may occur by transfer between cells. However, a discussion of transfer between cells is not relevant to the relevant active step of the current invention - 'contacting'. A teaching that transfer 'may' occur between cells does not exclude the contacting of cells which is the relevant active method step of the claims of the current invention. In fact, the cited reference (Patton et al.) supports known mechanisms in which cells are contacted. For example (page 341 2nd column), the reference discusses a 'random walk' process. Since diffusion is a random process molecules are going to diffuse in a random fashion, not in a fashion such that all molecules go between the cells while none of the molecules contact the cells. There is no support for a mechanism in which all molecules preferentially transport in a pathway such that none of the molecules touch the cells and the molecules only transport between cells.

Appelants refer to an alternate uptake mechanism involving phagocytosis with respect to the '497 patent. However, example 1 (which was cited previously, including page 5 line 3 of the April 18, 2007 office action) of '497 involves instillation in the lungs of sheep, not phagocytosis. As such, arguments about phagocytosis are not applicable to example 1. An alternate embodiment does not constitute a teaching away (MPEP section 2123 II). Therefore, example 1 of '497 teaches the active steps of the current invention. Furthermore, the mechanism involved in

uptake has no bearing on the instant claims since the patent teaches all of the active method steps. Again it is reiterated that the patent teaches the same composition and a mode of administration that would result in "contacting". Thus the mechanism of cellular uptake would necessarily be the same.

Regarding Appelants arguments that certain claim limitations (claims 4,11-13,33,38) are not met, it is noted that section 2111.04 of the MPEP states:

> Claim scope is not limited by **claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure**. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:
> (A) " adapted to " or "adapted for " clauses;
> (B) " wherein " clauses; and
> (C) " whereby " clauses.

In the instant case, claim 13 recites 'wherein DKP does not engage a toll-like receptor'. The wherein clause "does not require steps to be performed" and "does not limit a claim to a particular structure". As such, the claim limitations are met by the prior art even if the prior art does not expressly teach that the methods do not engage a toll-like receptor. Claim 38 recites 'wherein the cell is contacted with the complex in a schedule resulting in substantially no increase in the cell's immune response'. Claim 4 recites 'wherein the immune response is increased by less than 20% in the presence of DKP compared to in its absence'. Claim 33 recites 'wherein following the plurailty of contacting steps, immune cells in the pulmonary tissue are non-responsive to subsequent contact with the compound'. Since schedules (a single administration could be interpreted to be a schedule) and a plurality of contacting steps (compare claim 33 of the current invention) are taught in the prior art ('497 in example 1 – contacting in each lung; '885 in example 2 and claim 6 – contacting prior to meals) the active steps of claims

4,33,38 are taught. Although Appelants point to an embodiment in which an antigen is used, it is an alternate embodiment and not representative of the examples (in which calcitonin is used in example 1 of '497 or in which insulin is used in example 2 of '885) and does not constitute a teaching away (MPEP section 2123 II). It is noted that all of the claims in question do not recite additional active steps on how to achieve the prevention of an increase in a cell's immune response. Hence, arguments drawn to the disclosure not relating to the prevention of an increase in a cell's immune response are drawn to an unclaimed feature. Therefore, the claim limitations (in particular claims 4,11-13,33,38) are met.

Appelants Arguments – 103 rejections

In addition to the above arguments for the 102 rejections, the Appelants make specific arguements regarding the 103 rejection with the '497 and '885 patents. Appelants argue that neither patent discloses a method for enhancing transport of a compound across a cell membrane and that one would not have a reasonable expectation of success. Appelants argue that no motivation is provided to combine the references. Appelants argue that the '497 patent teaches away from not increasing a cells immune response since it discloses methods for increasing a cells response.

Response to Arguments—103 rejections

Appelants argue that one would not have reasonable expectation of success for enhancing transport. In addition to the reasons set forth above, the '885 patent expressly teach enhanced transport: 'formulations and methods also are provided for the improved transport of active

agents across biological membranes' (abstract and column 3 line 42). Further, it is stated that 'the diketopiperazines also serve both to stabilize and enhance delivery to the entrapped materials. Formulations also have been developed for the enhanced transport of active agents across biological membranes' (column 4 line 12). Therefore, one would have a reasonable expectation of success based on the express teaching of '885.

Although Appelants argue that there is no motivation to combine the references, one would be motivated to combine the references because '497 itself is referenced in '885 (column 2 line 58) and mentioned as work to improve upon (column 2 last paragraph through column 3 first paragraph). Therefore, one would have been motivated to combine the references based on the express teaching of '885. Further, both references are focused on similar subject area and directed to solving the same problem as both references teach compounds comprising an active agent encapsulated with DKP microparticles for administration for active targeting of pulmonary tissue.

Although Appelants point to an embodiment in which an antigen is used, it is an alternate embodiment and not representative of the examples (in which calcitonin is used in example 1 of '497 or in which insulin is used in example 2 of '885) and does not constitute a teaching away (MPEP section 2123 II).

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

1/22/08

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